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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,201	04/25/2001	Susan Salceda	DEX-0196	2155

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EXAMINER
DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
1642	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,201	SALCEDA ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *2-6 and 8-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 06/10/01 01/29/03
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election with traverse of group VIII, claims 1, 7, SEQ ID NO:8, species cells and tissues in Paper No. 9 is acknowledged. The traversal is on the ground(s) that 1) Restriction requirement is not proper, because a search for prior art relating to a CSG of groups 1-20 should also reveal art relating to the gene product encoded thereby and use thereof of groups 21-240, and thus it does not appear that a serious burden would be placed upon the Examiner if all the groups are searched together, and because no class or subclass numbers have been defined by the Examiner for any of the groups, and thus there is no evidence that the groups have acquired separate status in the art, nor that the searches for the groups are not co-extensive, 2) Any search of prior art related to diagnostic methods for prostate cancer using a specified CSG would reveal references teaching diagnostic methods in cells and tissues as well as bodily fluids, and thus it does not appear that a serious burden would be placed upon the Examiner to search for both cells and tissues and bodily fluids. In addition, Applicant requested that at least SEQ ID NO:7 is rejoined with SEQ ID NO:8.

It is noted that this application is a 371 application, and no class and subclass designation for different groups is required.

The arguments have been considered but are not found persuasive because of the following reasons: 1) Restriction requirement is proper, because groups 21-240 are either additional methods which do not recited SEQ ID NO:8, or additional use of SEQ ID NO:8, and because the searches for different groups are complex and require the

use of several database and are not based solely on classification search. Therefore, the searches for these patentably distinct groups 1-240 are not coextensive, and it would be a burden for the Examiner to search all the groups together, 2) The species restriction is proper, because different species do not share the same structure, and thus the searches for these species are not co-extensive, and it would be a burden for the Examiner to search all the species together.

The requirement is still deemed proper and is therefore made FINAL.

After review and reconsideration, SEQ ID NO:7 is rejoined with SEQ ID NO:8.

Accordingly, claims 1, 7, SEQ ID NO:7 or 8, species cells and tissues are examined in the instant application, wherein claims 1, 7 are examined only to the extent of a method for diagnosing the presence of prostate cancer, comprising determining mRNA level, and not protein level, of CSG (SEQ ID NO:7 or 8) in cells or tissues of a patient.

INFORMATION DISCLOSURE STATEMENT

It is noted that the references from the information disclosure statements of paper Nos: 6, 8, 10 of 01/15/02, 06/17/02 and 08/05/02, respectively, are missing and could not be considered. Applicant is invited to resubmit said references.

OBJECTION

1. Claim 1 is objected to because part of claim 1 encompasses non-elected inventions, i.e. a method for diagnosing the presence of prostate cancer, comprising

determining the non-elected protein level of CSG (cancer specific gene) of SEQ ID NO: 7 or 8, and determining the mRNA and protein levels of non-elected CSG of SEQ ID No:1-7, 9-20.

2. Claim 1 is objected to because claim 1 uses the abbreviation "CSG". A full name of CSG, i.e. cancer specific gene, is required to obviate this objection.

3. Claim 1 is objected to for the use of the language "normal" human control. It is not clear what constitutes "normal".

4. Claim 7 is objected to because claim 7 depends on non-elected claims 2-6.

5. Claim 7 is objected to because part of claim 7 encompasses non-elected inventions, i.e. a method for diagnosing the presence of prostate cancer, comprising determining the mRNA level of non-elected sequences of SEQ ID Nos:1-6, 9-20, and the protein level of the polypeptides encoded by SEQ ID Nos: 1-20.

Claim Rejections - 35 USC § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTON

The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

Claim 1 is drawn to a method for detecting the presence of prostate cancer, comprising determining the mRNA level of CSG in cells or tissues of a patient , wherein

a change in said level in said patient versus normal human control is associated with prostate cancer.

The specification discloses that CSG means the native mRNA encoded by the gene comprising SEQ ID NO:7 or 8, the levels of the gene comprising SEQ ID NO:7 or 8, or the level of a polynucleotide which is capable of hybridizing under stringent conditions to the antisense sequence of SEQ ID NO:7 or 8 (p.3, last paragraph, bridging p.4). The specification further discloses that the mRNA of Pro 115 (SEQ ID NO:7 or 8) is overexpressed in prostate cancer tissue case Nos: 1, 5 and 8, and underexpressed in prostate cancer tissue case No: 4, as compared to matching normal adjacent tissue (table 8 on pages 28-29).

It is noted that a polynucleotide which is capable of hybridizing under stringent conditions to the antisense sequence of SEQ ID NO:7 or 8 encompasses unrelated sequence of any structure and length, provided it shares a fragment sequence with SEQ ID NO:7 or 8, wherein via the common fragment, said unrelated sequence is capable of hybridizing under stringent conditions to the antisense sequence of SEQ ID NO:7 or 8.

Further, it is noted that CSG also means a gene comprising SEQ ID NO:7 or 8, wherein the structure of said gene is not disclosed in the specification.

The claims, as written, thus, encompass polynucleotides which vary substantially in length and also in nucleotide composition.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of

subgenera including full-length genes. A description of a genus of cDNAs may be acheived by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural freatures common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive strutural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the gene. The art indicates that the structures of genes with naturally occurring regulatory elements and untranslated regions is empirically determined (Harris et al. J. of The Am Society of

Nephrology 6:1125-33, 1995; Ahn et al. Nature Genetics 3(4):283-91, 1993; and Cawthon et al. Genomics 9(3):446-60, 1991). Therefore, the structure of these elements is not conventional in the art and one skilled in the art would therefore not recognize from the disclosure that applicant was in possession of the genus of nucleic acid, including genes, comprising SEQ ID NO: 7 or 8.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific nucleotide sequences and the ability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed. Thus, only a method for detecting the presence of prostate cancer, comprising determining the mRNA level of a polynucleotide sequence comprising SEQ ID NO: 7 or 8, but not the full breadth of the claims meet the written description provisions of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112, FIRST PARAGRAPH, SCOPE

1. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting the presence of prostate cancer, comprising determining the mRNA level of SEQ ID No:7 or 8 in prostate tissues, using as probes SEQ ID Nos: 27 and 28, does not reasonably provide enablement for a method for detecting the presence of prostate cancer, comprising determining the level of "CSG". The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is drawn to a method for detecting the presence of prostate cancer, comprising determining the level of CSG in cells or tissues of a patient, wherein a change in said level in said patient versus normal human control is associated with prostate cancer.

The specification discloses that CSG means the native mRNA encoded by the gene comprising SEQ ID NO:7 or 8, the levels of the gene comprising SEQ ID NO:7 or 8, or the level of a polynucleotide which is capable of hybridizing under stringent conditions to the antisense sequence of SEQ ID NO:7 or 8 (p.3, last paragraph, bridging p.4). The specification further discloses that the mRNA of Pro 115 (SEQ ID NO:7 or 8) is overexpressed in prostate cancer tissue case Nos: 1, 5 and 8, and underexpressed in prostate cancer tissue case No: 4, as compared to matching normal adjacent tissue (table 8 on pages 28-29).

It is noted that a polynucleotide which is capable of hybridizing under stringent conditions to the antisense sequence of SEQ ID NO:7 or 8 encompasses unrelated sequence of any structure and length, provided it shares a fragment sequence with SEQ ID NO:7 or 8, wherein via the common fragment, said unrelated sequence is capable of hybridizing under stringent conditions to the antisense sequence of SEQ ID NO:7 or 8.

The claim encompasses a method for detecting the presence of prostate cancer, comprising determining the mRNA level of polynucleotides comprising non-disclosed

nucleic acid sequences attached to the polynucleotide of SEQ ID NO:7 or 8, that is polynucleotides that hybridize to said polynucleotide of SEQ ID NO:7 or 8 under stringent conditions. However, neither the specification nor the claims define what is meant by stringent conditions. As conventionally understood in the art and as taught by US Patent No. 5,912,143, hybridization is used to refer to any process by which a strand of nucleic acid binds with a complementary strand through base pairing (col 5, lines 3-5) and further teaches that numerous equivalent conditions may be employed to comprise either low or high stringency conditions and hybridization solutions my be varied to generate conditions of either low or high stringency (col 5, lines 57-67). The stringent conditions claimed read on both high and low stringency conditions. It is well known that the lower the stringency condition the more dissimilar the hybridizing molecule will be from the molecule to which it hybridizes. When given the broadest reasonable interpretation, the claims are clearly intended to encompass a variety of species including full-length cDNAs, genes and protein coding regions. Clearly, it would be expected that a substantial number of the hybridizing molecules encompassed by the claims **would not** share either structural or functional properties with the polynucleotide of SEQ ID NO:7 or 8 .

Further, the claim as written, encompasses a method for detecting the presence of prostate cancer, comprising determining the level of a "gene" comprising SEQ ID NO:7 or 8 in cells or tissues of a patient , wherein a change in said level in said patient versus normal human control is associated with prostate cancer.

One cannot extrapolate the teaching of the specification to the scope of the claims because although the level of mRNA of SEQ ID NO:7 or 8 is increased or decreased in prostate cancer tissues, it is unpredictable that the level of a gene comprising SEQ ID No: 7 or 8 would be amplified or reduced. It is well known in the art that there is no correlation between the level of a gene and the level its mRNA. For example, van de Vijver, M et al, 1987, Mol Cell Biol, 7(5) : 2019-2023, teach that although the oncogene c-erbA is amplified mammary tumors, mRNA of c-erbA is not detected in mammary tumors (abstract and page 2020, second paragraph).

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

2. Claims 1, 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting the presence of prostate cancer, comprising determining the mRNA level of SEQ ID No:7 or 8 in prostate tissues, using as probes SEQ ID Nos: 27 and 28, does not reasonably provide enablement for a method for detecting the presence of prostate cancer, comprising determining the mRNA level of a CSG (cancer specific gene) or SEQ ID NO:7 or 8, in "any cell or any tissues", using "any probe". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 7 are drawn to a method for detecting the presence of prostate cancer, comprising determining the mRNA level of CSG which is SEQ ID No:7 or 8 in cells or

tissues of a patient , wherein a change in said level in said patient versus normal human control is associated with prostate cancer.

Claims 1, 7 encompass a method for detecting the presence of prostate cancer, comprising determining the mRNA level of CSG or SEQ ID No:7 or 8 in any cell or any tissue of a patient, i.e. detecting mRNA level of SEQ ID NO:7 or 8 in metastatic prostate cancer cells or tissues other than primary prostate cancer tissues, wherein a change in said level in said patient versus normal human control is associated with prostate cancer.

Further, claims 1, 7 encompass a method for detecting the presence of prostate cancer, comprising determining the mRNA level of CSG which is SEQ ID No:7 or 8 in any cell or any tissue of a patient, using any probe which is not necessarily specific for SEQ ID NO:7 or 8.

The specification discloses that the mRNA of Pro 115 (SEQ ID NO:7 or 8) is overexpressed in prostate cancer tissue case Nos: 1, 5 and 8, and underexpressed in prostate cancer tissue case No: 4, as compared to matching normal adjacent tissue (table 8 on pages 28-29).

One cannot extrapolate the teaching of the specification to the scope of the claims because it is unpredictable that prostate cancer cells metastasized to cells or tissues other than the primary prostate cancer tissues still express the claimed sequences, because expression of a sequence could be lost during the progression toward metastasis. For example, Kibel, AS et al, 2000, J urol, 164(1): 192-6 teach that gene expression in the chromosomal region 12p12-13 is different in primary and

metastatic cells, and that inactivation in the chromosome region 12p12-13 occurs prior to metastasis. Ren, C et al, 1998, Cancer Res, 58(6): 1285-90, teach a loss of expression of lysyl oxidase mRNA during progression to metastasis. Gingrich, JR et al, 1996, Cancer res, 56(18): 4096-4102 teach a loss of normal E-cadherin expression as primary tumors become less differentiated and metastasize.

Thus in view of the above, one would not have expected that the claimed sequence would be detected in any cell or tissue.

Further, although the specification discloses the use of the probes of SEQ ID Nos:27 and 28 (p.27, lines 15-20) for detection of SEQ ID NO:7 or 8, as written, no specific probes are recited in the claims for use in the detection of SEQ ID NO:7 or 8. One would have expected that using any probe, non-related nucleic acid sequences, which share some similarity with SEQ ID NO:7 or 8, could be detected, e.g. epitheliasin, which is 99.6% similar to SEQ ID NO:8, from nucleotide 22 to 3222 (Jacquinet E et al, 2001, Eur J Biochem, 268 (9): 2687-2699, and MPSRCH sequence similarity search report, 2003, us-09-807-201-8.rge, pages 7-8). Epitheliasin is strongly detected in normal prostate, as taught by Jacquinet E et al and thus could effect the total level of mRNA detected. In other words, using any probe, it is unpredictable that one could detect a change in the mRNA level of SEQ ID NO:7 or 8 in prostate cancer as compared to normal control, due to possible interference by other unrelated sequences that are also detected.

same for FP.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention as broadly as claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

MINH TAM DAVIS

January 31, 2003